Infections Associated with United States Travel

Caytlin A. Deering, DO
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Objectives

- Develop a strategy for taking a thorough and relevant travel history
- Recognize, identify, and treat human infections associated with travel within the United States
- Discuss prevention of infections associated with United States travel

Outline

- Travel history
- Tick-borne Infections
- Mosquito-borne Infections
- Endemic Mycoses
- Other Infections
“If you reject the food, ignore the customs, fear the religion and avoid the people, you might better stay at home.”

- James Michener
Ask Questions About Travel

- Who?
- Why?
- What?
- Where?
- When?

TRAVELER

Obtain a Travel History

- Who?
  - Sexual Partners
  - Inmates, Shelters
- What?
  - Activities
  - Exposures (Foods, Animals)
- When?
  - Time of year
  - Duration
- Where?
  - Travel Itinerary
  - Accommodations
- Why?
  - Leisure
  - Work
Tick-borne Infections

- *Ixodes scapularis* (Deer Tick)
- *Amblyomma americanum* (Lone Star Tick)
- *Dermacentor variabilis* (Dog Tick)

**Lyme Disease**

- *Borrelia burgdorferi*
- Vector: *Ixodes scapularis* (deer tick)
- Northeast, Mid-Atlantic, Upper Midwest
- 28,453 confirmed and 9,616 probable cases in 2015
  - Most common tick-borne illness in U.S.
Lyme Disease

- Early infection
  - Erythema Migrans
  - Constitutional symptoms
- Early disseminated disease
  - Multiple Erythema Migrans, constitutional symptoms
  - Neurologic (12-14%)
    - Cranial nerve palsies (CN VII)
    - Aseptic meningitis
    - Radiculitis
  - Carditis (1%)
    - A-V block
- Late Lyme disease
  - Arthritis
  - Neurologic
    - Encephalitis, Encephalopathy, sensory peripheral neuropathy

https://www.cdc.gov/lyme/stats/index.html
Lyme Disease

Erythema Migrans (target lesion)

Diagnose Lyme Disease

- Early Infection
  - Clinical diagnosis

- Early Disseminated Infection
  - Clinical findings
  - Positive Serology
    - EIA and Western Blot

- Late Infection
  - Clinical condition
  - Positive serology
  - CSF testing for Lyme antibody
  - Synovial fluid *B. burgdorferi* PCR
Erythema Migrans Treatment

- Doxycycline 100mg BID x14 days
- Amoxicillin 500mg TID x14 days
- Cefuroxime 500mg BID x14 days

- Alternative treatments
  - Azithromycin 500mg x10 days
  - Clarithromycin 500mg BID x21 days

Lyme Disease Treatment

- Cranial Nerve Palsy
  - Oral regimen (14-28 days)
- Meningitis
  - Intravenous ceftriaxone (10-28 days)
- Cardiac Disease
  - Ceftriaxone until heart block resolves
  - Oral regimen to complete course (14-21 days)
- Late Lyme Arthritis
  - Oral regimen (28 days)
Anaplasmosis
Human granulocytotrophic anaplasmosis (HGA)

- *Anaplasma phagocytophilum*
- Vector: *Ixodes scapularis* (deer tick)
- Northeast, Upper Midwest
- 1,761 reported cases in 2010
Anaplasmosis

- Incubation period of 1-2 weeks
- Symptoms
  - Fever
  - Headache
  - Myalgias
  - Nausea, vomiting
- Maculopapular rash (~10%)
- Laboratory abnormalities
  - Elevated liver enzymes
  - Leukopenia, thrombocytopenia
Anaplasmosis Diagnosis and Treatment

- Serology
  - Single titer > 1:256, or four-fold increase in titer
  - Acute testing often negative
- PCR on whole blood
- Visible morulae in granulocytes (25-75%)

Doxycycline (10 day course)
Alternative: Rifampin

Anaplasmosis

Morulae in granulocyte
Babesiosis

- *Babesia microti*
- Vector: *Ixodes scapularis* (deer tick)
- Northeast, Midwest, West Coast
- 1,744 cases reported in 2014
- Most commonly transfused pathogen
  - 159 cases (1979-2009)

*Number of reported cases of babesiosis, by county of residence — 31 states, 2014*
Babesiosis

- 1-6 week incubation period
- Symptoms
  - Fever, flu-like symptoms, cough
- Laboratory abnormalities
  - Hemolytic anemia, thrombocytopenia
  - Elevated liver enzymes
- Severe illness
  - Elderly, immunocompromised, asplenic patients
  - Parasitemia >10%
  - Severe hemolysis
  - Liver, kidney, or respiratory failure

Babesiosis Diagnosis

- Thick and thin blood smears
  - Intraerythrocytic ring forms
  - Maltese cross
- PCR on whole blood
  - Most sensitive
- Serology
  - IFA IgM >1:64
  - Four-fold increase in titer
Babesiosis

Intraerythrocytic ring forms

Maltese Cross (tetrad)

Babesiosis Treatment

- Asymptomatic
  - No treatment required
  - Atovaquone and azithromycin (7 days)
    - Persistent parasitemia
- Mild-moderate disease
  - Atovaquone and azithromycin (7-10 days)
  - Adverse drug reactions (15%)
- Severe disease
  - Clindamycin + quinine (7-10 days)
  - Adverse drug reactions (72%)
- Critically Ill
  - Exchange blood transfusions
    - Parasitemia >10%, severe anemia, liver, kidney, respiratory failure
Powassan encephalitis

- Powassan virus
  - Flavivirus, recognized in 1958
- Vector: *Ixodes* spp. (deer tick), *Dermacentor andersoni* (wood tick)
- Northeastern and North-central states
- Symptoms
  - Fever, headache, seizure, focal neurologic signs, altered mental status

Treatment: Supportive care
Ehrlichiosis
Human monocytotropic ehrlichiosis (HME)

- *Ehrlichia chaffeensis*
- Vector: *Amblyomma americanum* (Lone Star tick)
- Southeastern and South-Central states
- ~800-1,000 cases annually


https://www.cdc.gov/ticks/tickborne_diseases/ehrlichiosis.html
Ehrlichiosis

- 5-15 day incubation period
- Symptoms
  - Fever, headache, abdominal pain, nausea
  - Meningitis (20%)
  - Maculopapular rash (~30%)
- Laboratory abnormalities
  - Elevated liver function tests, thrombocytopenia, leukopenia
- Severe illness
  - Elderly, immunocompromised, asplenic patients
  - Liver, kidney, or respiratory failure
  - Coagulopathies

Ehrlichiosis Diagnosis and Treatment

- Serology
  - Single titer > 1:256, or four-fold increase in titer
  - 85% negative during first week
- PCR whole blood
- Visible morulae in monocytes or lymphocytes (2-38%)

Don’t wait for confirmation, treat if suspected!
Doxycycline (10 day course)
Alternative: Rifampin
Ehrlichiosis

Morulae in monocyte

Southern Tick-Associated Rash Illness (STARI)

- Unknown cause
  - Previously thought *B. lonestari*
- Vector: *Amblyomma americanum* (Lone Star tick)
- Southeastern and south-central states
- Symptoms
  - > 8 cm rash near bite
  - Fevers, headache, malaise

Treatment: Often treated with antibiotics
Rocky Mountain Spotted Fever (RMSF)

- *Rickettsia rickettsii*
- Vector: *Dermacentor variabilis* (dog tick), *Dermacentor andersoni* (wood tick)
- South-central, Southeastern, Mid-Atlantic
- 500-1000 cases reported annually

Incidence for Spotted Fever Rickettsiosis (2014)

[Map showing incidence of RMSF cases per million across the United States]

https://www.cdc.gov/rmsf/index.html
Rocky Mountain Spotted Fever

- Incubation period 3-12 days
- Symptoms
  - Fever, headache, malaise
  - Petechial rash develops 3-5 days later
    - Found on palms and soles
  - Neurologic involvement common
- Laboratory abnormalities
  - Hyponatremia, thrombocytopenia, elevated liver function tests

Petechial rash of RMSF
**RMSF Diagnosis and Treatment**

- Serologic testing
  - Seroconversion 7-10 days after onset
  - IFA is the standard, cross reactivity seen

**Do not wait for confirmatory testing!**

- Doxycycline (7 days)
- Alternative: Chloramphenicol

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**Colorado Tick Fever**

- Colorado tick fever virus
- Vector: *Dermacentor andersoni* (wood tick)
- Mountain West
- Symptoms
  - Fever, headache, leukopenia, thrombocytopenia, biphasic course

**Treatment: Supportive care**
Tick-borne Relapsing Fever (TBRF)

- *Borrelia hermsii, B. parkeri, B. turicatae*
- Vector: *Ornithodoros spp.*
- Western mountains and deserts
- Symptoms: high fevers, chills, headache, relapsing course
- Treatment
  - Often self-limited
  - Doxycycline (5-10 days)
  - Ceftriaxone if evidence of meningitis

Prevention of Tick-borne Infections

- Avoid Tick Contact
- Tick Removal
  - 24-36 hours for Lyme Disease
  - 4-6 hours for RMSF
- DEET
- Permethrin
  - clothes, tents
Summary of Tick-borne Infections

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<td>Ornithodoros spp.</td>
<td>Doxycycline</td>
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Mosquito-borne Infections

*Aedes aegypti*
Yellow fever mosquito
West Nile Virus (WNV)

- Mosquito-borne flavivirus
  - Highest risk June-November
- 33 states, 67 cases in 2017
  - 40 cases of neuroinvasive infection
- Asymptomatic Infection (80%)
- WNV Fever (20%)
  - Fever, headache, rash
- WNV neuroinvasive infection (1%)
  - Encephalitis
  - Aseptic Meningitis
  - Myelitis

West Nile Virus Activity by State (July 25, 2017)

[Map of West Nile Virus activity by state](https://www.cdc.gov/westnile/statsmaps/preliminarymapdata2017/activityystate.html)
WNV Diagnosis and Treatment

- WNV IgM antibody
  - Serum, CSF
  - Cross-reactivity with other flaviviruses

Treatment: Supportive Care
Report WNV to Health Department

Zika Virus

- Mosquito-borne arbovirus
  - *Aedes aegypti*

- Modes of Infection
  - Mosquito bite
  - Vertical transmission
  - Sexual transmission
  - Blood transfusion
Zika Virus in the United States

- Brownsville, Texas
  - Zika cautionary area since December 2016
- Miami-Dade County, Florida
  - Zika cautionary status removed June 2, 2017

Brownsville, TX


Brownsville, TX. Yellow shows areas where pregnant women should consider postponing travel.
Miami-Dade County, FL


Zika Virus

■ 80% of infections are asymptomatic
■ Mild Illness – 95% of symptomatic infections
  □ Fever, arthralgia, conjunctivitis
  □ Diffuse maculopapular rash
    ■ Pruritic, spares palms and soles
■ Symptoms last up to one week

Treatment: Supportive Care
Zika Virus Prevention and Safety

- DEET containing repellants
- Mosquito Control
- Zika and Pregnancy
  - Avoid travel where Zika transmission is a concern
  - Pregnancy avoidance
    - 6 months from last possible exposure for men
    - 2 months from last possible exposure for women

Endemic Mycoses
Blastomycosis

- *Blastomyces dermatitidis*
  - Dimorphic fungus
  - Moist, acidic soil
- Southeast and South-Central states, Midwest
  - Hunters, farmers, manual laborers
  - Wisconsin reports highest incidence
    - 10-40 cases/year
Blastomycosis

- Infection by Inhalation
  - Pneumonia
  - Disseminated disease

- Diagnosis
  - Culture
  - Urinary antigen, serum antigen
    - Cross-reactivity seen
  - Large yeast with broad based bud
- Serologic testing not recommended

Blastomycosis

- Pulmonary disease (70-75%)
  - Asymptomatic (50%)
  - Acute disease resembles bacterial pneumonia
  - Chronic disease resembles malignancy or tuberculosis

- Cutaneous
  - Papules on the face
  - Ulcerative lesions

- Bones
  - Osteomyelitis

- Genitourinary
  - Prostatitis, epididymitis
- CNS infection is rare
Blastomycosis Treatment

- Severe Pulmonary Infection
  - Amphotericin B, itraconazole
- Disseminated Infection
  - Itraconazole
- Duration of therapy: 6-12 months

Coccidioidomycosis

- *Coccidioides immitis*
  - Dimorphic fungus
  - Warm, dry environments, deserts
- San Joaquin Valley
  - Most cases in CA, AZ
- Approximately 150,000 infections/year
Coccidioidomycosis

- Infection by inhalation
- Presents as acute or sub-acute pneumonia
  - Incubation period 7-21 days
  - Cough, fever and infiltrate
  - Asymptomatic with X-ray findings
- Skin lesions
  - Erythema Nodosum
- Bone infection
- CNS infection
  - Sub-acute or chronic

Areas Endemic for Coccidioidomycosis

- Highly endemic
- Established endemic
- Suspected endemic
Coccidioidomycosis Diagnosis and Treatment

- Diagnosis
  - Spherule identification
  - Positive fungal culture
  - Positive serologic testing

- Treatment
  - Most resolve symptoms without treatment
  - Fluconazole, itraconazole
  - Duration: 3-6 months

Histoplasmosis

- *Histoplasma capsulatum*
  - Dimorphic fungus
  - Soil, associated with birds and bats
- Ohio and Mississippi River Valleys
- 6.1 cases/100,000 persons in the Midwest
Histoplasmosis

- Infection by inhalation
  - Acute Infection
  - Reactivation
- Pulmonary Infection
  - Acute, chronic
- Disseminated
  - Bone marrow, gastrointestinal tract
- CNS
  - Meningitis, abscess
- Mediastinitis
- Pericarditis
- Ocular
Histoplasmosis Diagnosis and Treatment

- Diagnosis
  - Urinary or Blood Antigen

  Severe pulmonary infection
  - Amphotericin B, itraconazole

Mild-moderate pulmonary infection
  - Usually self-limited
  - Itraconazole

Other Infections

- *Giardia lamblia*
- *Deer mouse*
- *Naegleria fowleri*
Giardiasis

- **Giardia lamblia**
  - Flagellated, bi-nucleated protozoan
- Most common intestinal parasite in North America
- Contaminated water or food, fecal-oral route
  - Surface water easily contaminated
  - Highly contagious
    - 10 cysts to be infective

Giardiasis

- Incubation period 1-2 weeks
- Presentation
  - Acute diarrhea
  - Chronic diarrhea with malabsorption
- Symptoms
  - Abdominal pain
  - Nausea, vomiting
  - Large volume stool, watery, foul smelling
Giardiasis Diagnosis

- Direct fluorescent assay of stool
  - Most sensitive and specific
- Fecal ova and parasite exam
- Antigen testing, PCR tests
- Duodenal aspirate to examine for trophozoites
Treatment

- Metronidazole 250mg PO TID x7 days
- Tinidazole 2g PO x1 dose
- Nitazoxanide 500mg PO BID x3 days
- Paromomycin in pregnancy

Primary Amebic Meningoencephalitis (PAM)

- *Naegleria fowleri*
  - “brain eating ameba”
- Found in warm, fresh water
- Enters via nasal mucosa
- 4 survivors in 143 U.S. cases since 1962
PAM

- Symptoms begin 1-9 days after exposure
  - Death 1-18 days after symptom onset
- Symptoms
  - Headache, fever, nausea
  - Seizures, altered mental status, coma
- Diagnosis
  - High level of suspicion
  - *N. fowleri* organisms, nucleic acid, or antigen in CSF or tissue
PAM Treatment

- No standard treatment
  - Amphotericin B
  - Fluconazole
  - Miltefosine
  - Azithromycin
- Duration 9-30 days

PAM by State of Exposure 1962-2016
Hantavirus

- Sin Nombre virus
  - Discovered in 1993 after four-corners outbreak
- Reservoir: North American deer mouse
- Inhalation of virus that has been excreted in urine, saliva, or feces of rodents
- Risk Factors: high rodent density in home, handling rodents, occupational or recreational exposure

Hantavirus Symptoms

- Early Symptoms
  - Fevers, headache, myalgias
- Hantavirus Pulmonary Syndrome
  - 4-10 days after symptom onset
  - Cardiopulmonary symptoms, ARDS
  - Thrombocytopenia, leukocytosis, DIC
  - 50% mortality
Hantavirus Pulmonary Syndrome

https://www.cdc.gov/hantavirus/surveillance/state-of-exposure

Hantavirus Diagnosis and Treatment

- Hantavirus-specific IgM
  - Rising IgG
- Hantavirus-specific RNA by PCR
- Hantavirus-specific antigen
  - Tissue

Treatment: Supportive Care
Hantavirus Prevention

- Avoid rodent exposures
  - Recreational
  - Occupational
    - Agriculture, construction, forestry, cleaning
- Rodent Control
- Educational Materials

Rabies

- 55,000 people die annually from rabies
  - 3 human cases/year in the US
- Bats most frequently reported rabid animal
- Major risk groups
  - bats, raccoons, skunks, foxes

Treatment: HRIG then 4 dose vaccine schedule (Days 0, 3, 7, 14)
Hansen’s disease (Leprosy)

- *Mycobacterium leprae*
- Spread by droplet inhalation
  - 2-5 year incubation period
  - Sustained exposure to infected persons
- Hypo-pigmented skin lesions, loss of sensation in peripheral nerves
- 95% of the population is immune
- 178 new U.S. cases in 2015
  - Indigenous in LA, TX, MS, HI
Hansen’s Disease and Armadillos

- Natural reservoir
- Infection may be possible
  - Direct contact
  - Meat consumption

Other Diseases to Consider

- *Mycobacterium tuberculosis*
- HIV Infection
- Syphilis
- Tularemia
- Leptospirosis
- Acute Infectious Hepatitis
- Influenza
Questions

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